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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,257	04/27/2001	Karin Kellner	CIBT-P01-099	8923

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EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,257	KELLNER ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2 and 5-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 10/7/04, have been entered in full.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments, persuasive arguments and supporting evidence.

Applicant is notified that the finality of the previous Office Action (5/5/04) is withdrawn due to the issuance of the new rejection below.

It is noted that a Notice of Appeal has been filed. Applicant can request a refund for the associated fees or leave it as credit for future appeals.

New Rejection:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5844079 to Ingham et al. in view of U.S. Patent No: 6468978 to Esswein et al., filed April 28, 1999.

Ingham et al. disclose a method of making a cartilaginous prosthesis comprising seeding a polymeric matrix of articular chondrocytes and contacting the seeded construct with a naturally occurring hedgehog polypeptide, see col 50, particularly lines 40-68. Wherein the polymer matrix is polyglycolid acid (see col 50, L55); and a wherein the naturally occurring hedgehog polypeptide is hydrophobically modified, e.g. with a lipid moiety (see col 28, line 29). Ingham et al., however, do not explicitly teach that the concentration of the hedgehog protein be at least 500 pg/mL as specifically recited in claims 6 and 7. However, Ingham et al. does teach that the 19kDa N-terminal fragment becomes active at a concentration of about 5 to 50 pM (~100 to 1000 pg/mL), see col 106 Example 9. Thus, it would simply be a matter of routine optimization of operating parameters to use a concentration of at least 500 pg/mL(e.g. 1000 pg/mL) based on what was known of the activity of hedgehog proteins as taught by Ingham et al. when practicing the invention of Ingham et al., the motivation to do so is provided by Ingham who teach that hedgehog protein is active at a concentration of 1000 pg/mL.

Ingham et al. do not disclose that the hedgehog protein should be dipalmitoylated. Esswein et al. teach that dipalmitoylated hedgehog proteins exhibit much higher biological activity than non-modified hedgehog proteins (col 13, lines 31-37), and that such can be used advantageously to induce or stimulate chondrocytes (col 9, line 5).

Therefore, one of ordinary skill in the art, at the time the invention was made, and with reasonable expectation of success, would be motivated to use dipalmitoylated hedgehog proteins as taught by Esswein et al when practicing the method of making a cartilaginous prosthesis as taught by Ingham et al., the motivation to do so being provided by Esswein et al who teach that dipalmitoylated hedgehog proteins exhibit much higher biological activity than non-modified

hedgehog proteins, and that such can be used advantageously to induce or stimulate chondrocytes.

Applicant's arguments, as they may relate to the new rejection, have been thoroughly considered but not deemed persuasive. Specifically, Applicant alleges that the examiner has not provided any evidence that one of ordinary skill in the art would arrive at the particular concentrations and formulations recited in the claims. This argument has been fully considered but not deemed persuasive. Regarding the particular concentrations, it is old and well established in the art of Biology that assays are performed to determine the optimal concentrations of active components. Regarding the particular formulation, i.e. the dipalmitoyl moiety, Esswein et al provide the motivation for such, as discussed above.

Conclusion

Please note the new central fax number for official correspondence below:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961. Official papers filed by fax should be directed to 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

December 30, 2004

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER